REMARKS

Claims 1 through 16 and 20 through 26 were presented for examination in the present application. The instant amendment cancels claims 1 through 16 and 20 through 26 without prejudice and adds new claims 27 through 45. Thus, claims 27 through 45 are presented for consideration upon entry of the instant amendment.

Claims 8 through 12 were rejected under 35 U.S.C. 112, second paragraph. Claims 1 through 16 and 20 through 26 were rejected under 35 U.S.C. 112, first paragraph. Claims 1 through 7, 13 through 16, and 23 through 26 were rejected under 35 U.S.C. 103(a) as being unpatentable over Casarini et al. (Intl. J. Biochem Cell Biology 2001 Vol. 33, page 75-85) ("Casarini"). Claims 20 through 22 were rejected under 35 U.S.C. 103(a) as being unpatentable over Casarini in view of U.S. Patent No. 4,208,479 ("Zuk"). Claims 8, 9, 11, and 12 were rejected under 35 U.S.C. 103(a) as being unpatentable over Casarini in view of Hattori et al. Hypertension 2000 Vol. 35, pgs 1284-1290 ("Hattori").

In the interest of expediting prosecution and for purposes of clarity, Claims 1 through 16 and 20 through 26 have been cancelled and rewritten as new claims 27 through 45.

Reconsideration and withdrawal of the rejections to claims 1 through 16 and 20 through 26 are respectfully requested.

New claim 27 recites "A method of detecting a predisposition for the development of hypertension in an individual, comprising detecting a presence of at least three angiotensin converting enzyme isoforms (emphasis added)".

The claimed method of detecting a predisposition for developing hypertension in an individual comprising the step of detecting the presence of three angiotensin converting enzyme ("ACE") isoforms is supported in the Specification at least in paragraphs [0067] and [0068]. Both of these paragraphs disclose that normotensive individuals with hypertensive parents who presented the three ACE isoforms (65kDa, 90kDa, and 19kDa) were predisposed to develop hypertension later in life. On the other hand, normotensive individuals should only present the 65kDa and 190kDa, while hypertensive individuals present only the 65kDa and 90kDa isoforms. As such, the presence of the 90kDa isoform can be regarded as a marker for hypertension and the combination of the three isoforms indicates a predisposition to develop hypertension.

New claim 37 recites "A method of detecting a predisposition for the development of a kidney lesion in an individual, comprising: detecting a presence of at least three angiotensin converting enzyme isoforms... and quantifying the presence of the at least three antiotension converting enzyme isoforms (emphasis added)".

The claimed method of detecting a predisposition for the development of a kidney lesion in an individual, comprising detecting and quantifying the presence of the 65kDa, 90kDa, and 190kDa ACE isoforms, is supported in the Specification at least in paragraphs [0042] and [0095]. The Specification discloses that the ACE activity in urine is produced by the kidcney, and that any considerable increase of ACE activity can be used as a marker for detecting renal lesions. In addition, it is suggested that the high concerntration of ACE in urine was due to the local secretion site of this enzyme in the kidney (duct collector). In addition,

the Specification discloses in Table II, the tissue ACE activity distribution in adrenal, aorta, heart, liver, lung, kidney and testicles. This further supports the idea that these tissues are capable of producing ACE isoforms.

Applicants respectfully submit that new claims 27 and 37 have both novelty and our non-obvious over the cited art. Specifically, it would not be obvious for one of ordinary skill in the art to imagine that the three ACE isoforms (65kDa, 90kDa, and 190kDa) when presented in a normotensive individual, could be used as a marker for detecting a predisposition to develop hypertension and/or kidney lesions.

In Casarini, the presence of two ACE isoforms (65kDa and 90kDa) is detected in the urine of hypertensive patients.

In Hattori, the presence of the 190kDa and 65kDa isoforms is characterized in the urine of premature and full term newborn babies. It was shown that until the third postnatal week, the level of ACE isoform 190kDa was than that of the ACE isoform 65kDa, perhaps because of brush-border differentiation and renal maturation. These results suggest that ACE activity is related to renal development in humans. In previous studies, the inventors have also demonstrated that the ACE isoforms, 190kDa and 65kDa, could be detected in the urine of normotensive individuals.

However, in none of the cited art is it ever disclosed the simultaneous presence, in the same urine sample, of the three ACE isoforms.

In addition, while Casarini and Hattori disclose methodologies

to isolate the ACE isoforms, neither discloses or suggests the possibility of using the presence of the three ACE isoforms for detecting a predisposition for developing hypertension and/or kidney lesions.

Applicants respectfully submit, therefore, that based on the cited prior art, it would not have been obvious to one of ordinary skill in the art, to conjecture that an individual possessing the three ACE isoforms would have a greater chance of developing hypertension and/or kidney lesions.

In view of the above, it is respectfully submitted that the present application is in condition for allowance. Such action is solicited.

If for any reason the Examiner feels that consultation with Applicants' attorney would be helpful in the advancement of the prosecution, the Examiner is invited to call the telephone number below.

Respectfully submitted,

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Charles N. J. Ruggiero
Reg. No. 28,468
Attorney for Applicant(s)
Ohlandt, Greeley, Ruggiero & Perle, L.L.P.
One Landmark Square, 10th floor
Stamford, CT 06901-2682
Tel: (203) 327-4500
Fax: (203) 327-6401